



## Synovial stem cells and their responses to the porosity of microfibrous scaffold.

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## **Public Summary:**

In this study, we identified and characterized a new type of stem cells from the synovial membrane of knee joint, named neural crest cell-like synovial stem cells (NCCL-SSCs). NCCL-SSCs showed the characteristics of neural crest stem cells, and could differentiate into neural lineages as well as mesenchymal lineages. When treated with transforming growth factor beta1 (TGF-beta1), NCCL-SSCs differentiated into mesenchymal stem cells (MSCs) and lost the expression of Sox17 and the differentiation potential into neural lineages. To determine the responses of NCCL-SSCs to microfibrous scaffolds for tissue engineering, electrospun composite scaffolds with various porosities were fabricated. The increase in the porosity in microfibrous scaffolds enhanced cell infiltration in vitro and in vivo, but did not affect the morphology and the proliferation of NCCL-SSCs. Scaffolds with higher porosity increased the expression of cartilage and bone-forming genes but suppressed smooth muscle and fat forming genes. These results suggest that the differentiation of NCCL-SSCs can be controlled by both soluble chemical factors and biophysical factors such as the porosity of the scaffold. Engineering both NCCL-SSCs and scaffolds will have tremendous potential for tissue regeneration.

## Scientific Abstract:

Tissue-specific stem cells can be coaxed or harvested for tissue regeneration. In this study, we identified and characterized a new type of stem cells from the synovial membrane of knee joint, named neural crest cell-like synovial stem cells (NCCL-SSCs). NCCL-SSCs showed the characteristics of neural crest stem cells: they expressed markers such as Sox10, Sox17 and S100beta, were clonable, and could differentiate into neural lineages as well as mesenchymal lineages, although NCCL-SSCs were not derived from neural crest during the development. When treated with transforming growth factor beta1 (TGF-beta1), NCCL-SSCs differentiated into mesenchymal stem cells (MSCs), lost the expression of Sox17 and the differentiation potential into neural lineages, but retained the potential of differentiating into mesenchymal lineages. To determine the responses of NCCL-SSCs to microfibrous scaffolds for tissue engineering, electrospun composite scaffolds with various porosities were fabricated by co-electrospinning of structural and sacrificial microfibers. The increase in the porosity in microfibrous scaffolds enhanced cell infiltration in vitro and in vivo, but did not affect the morphology and the proliferation of NCCL-SSCs. Interestingly, microfibrous scaffolds with higher porosity increased the expression of chondrogenic and osteogenic genes but suppressed smooth muscle and adipogenic genes. These results suggest that the differentiation of NCCL-SSCs can be controlled by both soluble chemical factors and biophysical factors such as the porosity of the scaffold. Engineering both NCCL-SSCs and scaffolds will have tremendous potential for tissue regeneration.

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